Vilela et al., Biomater Med Appl 2018, 2:2
DOI: 10.4172/2577-0268.1000117

Biomaterials and Medical Applications

Review Article

A SCITECHNOL JOURNAL

Advances and Perspectives in Nanoscience and Technology Applied in Prognostics and Treatment of Cerebral Palsy

Diego N.Vilela[1], Paula von Randow Cardoso[2] and Hélio Ribeiro[3]*

Abstract

Due to the socioeconomic complexity unleashed by childhood cerebral palsy (CP), as well as other diseases, this subject needs to be better discussed and understood concomitantly with scientific and technological advances. In this context, this mini-review proposes to show how some different areas such as nanotechnology, bioinformatics, and artificial intelligence (AI) applied in the study of diseases can undoubtedly contribute to the elucidation or predicted of problems not yet well understood in medicine. Thus, this review points to some possible contributions that can collaborate with the prevention, early diagnosis and treatment of the diseases such as CP and others not so clear yet as well. In this context, it is also necessary to exemplify some advances in the nanoparticles used as drug-carrying agents, tumor markers and in the production of nanorobots with a broad spectrum of applications in nanomedicine. The elucidation of questions, for example in the CP is a good case correlated to these emerging areas with therapy and diagnosis medicine approaches, that should generate different decision-making by health experts with a view to prevention, recovery and improvement of the quality of life of patients.

Keywords

Biotechnology; Nanomedicine; Bioinformatics; Artificial intelligence; Nanoparticles; Carbon nanomaterials; Cerebral palsy

Introduction

Cerebral palsy (CP) can be defined as a group of permanent and non-progressive heterogeneous disorders in the development of movement body and posture, which may or may not be accompanied by sensory, muscular, cognitive, behavioral disorders, communication failures and epileptic problems [1,2]. In addition to being the most common cause of childhood disabilities, it has been estimated the prevalence between 2 and 2.5 cases per 1000 births [2,3], and this proportion has remained stable for more than 50 years [4]. Among its possible causes, some are commonly associated with birth asphyxia, intraventricular haemorrhage, hypoxic-ischemic encephalopathy, periventricular leukomalacia, intrauterine infections, restrictions on fetal growth and prematurity [4,5]. Due to its aetiology, the Gross Motor Function Classification System (GMFCS) and the Communication Function Classification System (CFCS) have been used to categorize, through levels, autonomous casual skills such as walking and sitting, as well as such as the ability to transmit information with family and third parties consecutively. Both these classifications varying from the first to the fifth level depending on the degree of dependence and communication, the first being milder and the fifth more severe [6,7]. Other forms of CP classification include the clinical (spastic, dyskinetic, ataxic), affected limbs (hemiparesis, diplegia, quadriplegia) and anatomical distribution, being unilateral (monoparetic, hemiparetic) and bilateral (diparetic, triparetic, quadriparetic) [7]. Regardless of the diagnosis be permanent or not, the impact on the life of the children and the people who around them it is critical, especially that of the mother since she normally dedicates her life to the child's care. This situation usually implies in psycho-social problems in children, leading them to situations of prejudice and isolation, which tends to worsen with their growth and gain in consciousness [2,3,8,9].

In addition to the permanent care, special treatments and assistance are necessary to keep the quality of life of the children and their caregiver, who are often the only sources of optimism and hope [2] but are usually tied to a high economic cost [7,9].

The information technology (IT) are growing up exponentiality in terms of an acquisition, storage and processing, with increasing speed, variety and availability, defining as Big Data [10]. This amount of information serves as fuel for the complex algorithms used in artificial intelligence, generating computational models capable of recognizing and classifying movement patterns, objects, sounds, as well as providing predictive models that support various decisions [11]. In this context, the application of such technology expands the way of seeing the past and the future of diseases that until they have been considered incurable [12].

In relation to body movement, corrective surgeries in children who have the classic "crouching gait" movement may have a better result if data obtained through adapted sensors to them (analyzed by biomechanical models) are used as decision support [13]. Thus, AI proves to be efficient in the classification of movements through a probabilistic approach with a high degree of precision, creating advantage in medical decisions [14]. With a similar technique, another application has been shown to be useful in monitoring and preventing the risk of intraventricular haemorrhage in analysis of heart rate and heart pressure in infants [15], as well as support to the doctor in the choice of cesarean section if there is risk in normal delivery [16]. Predictive models generate relevant information regarding the main factors associated with certain events, as in the case of severe scoliosis, pointing out important variables that contribute in a high gain of information about the disease, as well as the decrease of the uncertainty associated with the inferences of interest [17]. Through the use of bioinformatics resources, for example, the processing and understanding of DNA allows the comparison or search of genetic or epigenetic patterns for certain anomalies, associating some mutations that can cause CP, more specifically in the *ZC4H2* gene [4], as well as non-inherited punctual mutations (*de novo*) in the genes *KCNC3*, *ITPR1* and *SPTBN2*, which is related to the advancement of the parents' age to the ataxic form of CP [18], among other diseases. Another possibility that may provide us with hereditary arguments is the mutation in the *AP4M1* gene, described as congenital cerebral

***Corresponding author:** Hélio Ribeiro, Universidade Federal de Minas Gerais, Av. Antônio Carlos-Belo Horizonte, Brazil, Tel: +55 (31) 988886023; Email: helioribeiro@hotmail.com

Received: May 10, 2018 **Accepted:** June 01, 2018 **Published:** June 08, 2018

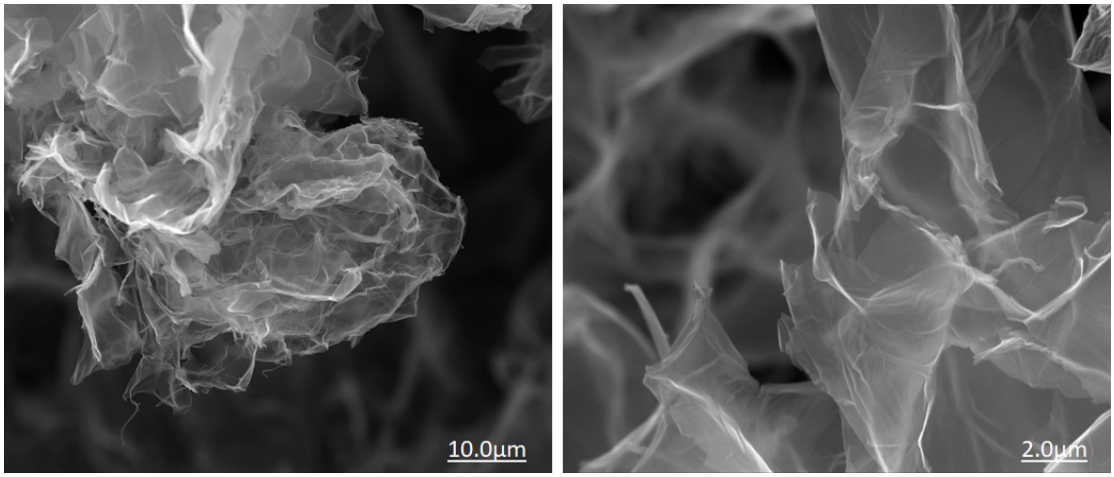

Figure 1: Scanning electron microscope (SEM) images of r-GO in different magnitude (Courtesy of Centro de Microscopia of Universidade Federal de Minas Gerais).

palsy, in which it mimics lesions in the white matter, usually acquired perinatally [19]. Another possibility is related to the use of biomarkers from a biotechnology perspective, that indicates situations where neonatal sepsis can occur [20], as well in the dysfunction of Excitatory Amino Acid Transporters 2 (EAAT2) case, as a consequence of the inefficient use of glutamate, that implies in neuronal development problems [21]. In addition, applications, such as Botulinum Toxin type A, which together with the conventional method of occupational therapy, significantly reduce muscle tone and improve the functionality of affected limbs [22].

The Nano science and nanotechnology have surprisingly created different ways of overcoming barriers and challenges posed by biology with its application in the field of medicine, with the study of biological devices, biosensors, drug delivery, nanorobots, and quantum dots used as contrast media, among others [23]. For instance, nanoparticles with different natures, such as dendrimers, have been used for systemic and therapeutic delivery, as in the case of N-acetyl-L-cysteine, previously widely used and with side effects in cases of intrauterine inflammation, significantly reducing premature birth rate [24]. Recent studies suggest that the therapy applied to the entire gestation process may, in addition to preventing the inflammatory response to the fetus, also enable the regeneration and repair of damaged areas, reducing the damage caused by the pathology [25].

In terms of nanomaterial, can be mentioned carbon nanotubes of graphene and their derivatives due to their exceptional physicochemical properties. For instance, the modified reduced graphene oxide (r-GO) has the capacity to momentarily cause the permeability of the Blood Brain Barrier (BBB), allowing the transport of substances to the central nervous system (CNS) directly, a procedure previously incapable of being performed by conventional methods (Figure 1) [26].

This methodology can help in inference of the degree of evolution in the treatment not only of the CP, but of all other pathologies that affect the CNS in some way, such as Parkinson's disease, multiple sclerosis, epilepsy and stroke, and have shown good results in protecting and reducing the impacts on their affected areas [27]. In addition, the r-GO presented low toxicity, excellent biological and physiological compatibility, efficiency as nanocarrier of drugs and genes in cancer treatment and gene therapy [28].

Conclusion

Advances in Nanoscience associated with computational techniques can collaborate synergistically in elucidation of problems and challenges posed by pathologies that affect the central nervous system, creating new paths and perspectives in diagnosis and therapy issues. The computational models associated with AI can be fundamental tools in the prediction of interfaces between nanoparticles and drugs, as well as the interaction between them in different biological environment. In this way, a great appeal and effort for the correlation these mentioned areas are necessary. This effort will directly result in improving the quality of life and dignity of people suffering from this condition and those who are at around of them. Clearly, prevention must be approached in an incisive way, since the hypothesis of cure for most diseases is non-existent.

Acknowledgement

Vilela thanks to the Centro de Microscopia of Universidade Federal de Minas Gerais-Brazil, for r-GO image courtesy.

References

1. Parisi L, Ruberto M, Precenzano F, Di Filippo T, Russotto C, et al. (2016) The quality of life in child with cerebral palsy. Acta Med Mediterr 32: 1665-1670.
2. Ribeiro MFM, Vandenberghe L, Prudente COM, Vila VSC, Porto CC (2016) Cerebral Palsy: how the child's age and severity of impairment affect the mother's stress and coping strategies. Cien Saude Colet 21: 3203-3212.
3. Pousada M, Guillamón N, Hérnandez-Encuentra E, Muñoz E, Redolar D, et al. (2013) Impact of Caring for a Child with Cerebral Palsy on the Quality of Life of Parents: A Systematic Review of the Literature. J Dev Phys Disabil 25: 545-577.
4. MacLennan AH, Thompson SC, Gecz J (2015) Cerebral palsy: causes, pathways, and the role of genetic variants. Am J Obstet Gynecol 213: 779-788.
5. Lee RW, Poretti A, Cohen JS, Levey E, Gwynn H, et al. (2014) A Diagnostic Approach for Cerebral Palsy in the Genomic Era. Neuromolecular Med 16: 821-844.
6. Bertule D, Vetra A (2014) The family needs of parents of preschool children with cerebral palsy: The impact of child's gross motor and communications functions. Medicina 50: 323-328.
7. Morilla CM, Caldas CACT, Scarpellini ACAV, dos Santos PL (2017) Family resources and promotion of development of children with cerebral palsy. J Hum Growth Dev 27: 166-174.

8. Reichman N, Corman H, Noonan K (2008) The impact of child disability on the family. Matern Child Health J 12: 679-683.
9. Chiluba BC, Moyo G (2017) Caring for a cerebral palsy child: a caregivers perspective at the University Teaching Hospital, Zambia. BMC Res Notes 10: 724.
10. Dolley S (2018) Big Data's role in precision public health. Front Public Health 6: 68.
11. Lerner I, Veil R, Nguyen D, Luu VP, Jantzen R (2018) Revolution in Health Care: How Will Data Science Impact Doctor–Patient Relationships?. Front Public Health 6: 99.
12. Zhang J (2017) Multivariate Analysis and Machine Learning in Cerebral Palsy Research. Front Neurol 8: 715.
13. Ku JP, Hicks JL, Hastie T, Leskovec J, Ré C, et al. (2015) The mobilize center: an NIH big data to knowledge center to advance human movement research and improve mobility. J Am Med Inform Assoc 22: 1120-1125.
14. De Laet T, Papageorgiou E, Nieuwenhuys A, Desloovere K (2017) Does expert knowledge improve automatic probabilistic classification of gait joint motion patterns in children with cerebral palsy? PloS One 12: 1-18.
15. Huvanandana J, Nguyen C, Thamrin C, Tracy M, Hinder M, et al. (2017) Prediction of intraventricular haemorrhage in preterm infants using time series analysis of blood pressure and respiratory signals. Sci Rep 7: 46538.
16. Fergus P, Hussain A, Al-Jumeily D, Huang D, Bouguila N (2017) Classification of caesarean section and normal vaginal deliveries using foetal heart rate signals and advanced machine learning algorithms. BioMed Eng OnLine 16: 89.
17. Bertoncelli CM, Bertoncelli D, Altamura P, Solla F (2017) PredictMed: Application of Big Data analysis in medical research. Orthop Spine Sports Med 1: 8.
18. Schnekenberg RP, Perkins EM, Miller JW, Davies WIL, D'Adamo MC, et al. (2015) De novo point mutations in patients diagnosed with ataxic cerebral palsy. Brain 138: 1817-1832.
19. Verkerk AJMH, Schot R, Dumee B, Schellekens K, Swagemakers S, et al. (2009) Mutation in the AP4M1 Gene Provides a Model for Neuroaxonal Injury in Cerebral Palsy. Am J Hum Genet 85: 40-52.
20. Buhimschi IA, Buhimschi CS (2010) The role of proteomics in the diagnosis of chorioamnionitis and early-onset neonatal sepsis. Clin Perinatol 37: 355-374.
21. Rajatileka S, Odd D, Robinson MT, Spittle AC, Dwomoh L, et al. (2018) Variants of the EAAT2 glutamate transporter gene promoter are associated with cerebral palsy in preterm infants. Mol Neurobiol 55: 2013-2024.
22. Lin Y, Huang C, Lin I, Shieh J, Chung Y, et al. (2015) Evaluating functional outcomes of Botulinum toxin type A injection combined with occupational therapy in the upper limbs of children with cerebral palsy: A 9-month follow-up from the perspectives of both child and caregiver. PLoS One 10.
23. Bhattacharya S (2018) Future of graphene in bio-medical application. J Nanomed Res 7: 186-187.
24. Lei J, Rosenzweig JM, Mishra MK, Alshehri W, Brancusi F, et al. (2017) Maternal dendrimer-based therapy for inflammation-induced preterm birth and perinatal brain injury. Sci Rep 7: 6106.
25. Balakrishnan B, Nance E, Johnston MV, Kannan R, Kannan S (2013) Nanomedicine in cerebral palsy. Int J Nanomedicine 8: 4183-4195.
26. Ribeiro H, Vilela DN, Almeida AH, Pinto MR (2018) Functionalized Graphene Process in Biotechnology: A Brief Landscape. J Nanomed Res 7: 00171.
27. Soni S, Ruhela RK, Medhi B (2016) Nanomedicine in Central Nervous System (CNS) Disorders: A Present and Future Prospective. Adv Pharm Bull 6: 319-335.
28. Shen H, Zhang L, Liu M, Zhang Z (2012) Biomedical Applications of Graphene. Theranostics 2: 283-294.

Author Affiliations

Top

[1]*Centro Universitário Barão de Mauá, R. Ramos de Azevedo, 423 - Ribeirão Preto, Brazil*

[2]*Fundação Ezequiel Dias, Rua Conde Pereira Carneiro, 80 - Belo Horizonte, Brazil*

[3]*Universidade Federal de Minas Gerais, Av. Antônio Carlos-Belo Horizonte, Brazil*